

USSN 09/215,095

Page 4

REMARKS

Claims 66 - 88 are pending in the instant application. Independent claims 66 and 83 have been amended; dependent claims 78 and 84 have been amended to conform the claims to the amendments to claims 66 and 83; and claims 89-98 have been added. No new matter is added by this amendment. Independent claim 66 recites a multi-layered granule comprising a single seed particle, a protein matrix layer, and an outer barrier or coating. Independent claim 83 recites a multi-layered granule comprising a single seed particle, an enzyme matrix layer, and an outer barrier or coating.

In this first office action final rejection, the Examiner continued his rejection of Applicants' claims 66 - 69, 72, 74, 78, 79, and 82 - 86 under 35 U.S.C. §102(b) as anticipated by Kiesser et al. (US Patent 5,739,091) and claims 75, 76, 80, 81, 87, and 88 under 35 U.S.C. §103(a) as being unpatentable over Kiesser et al. (US Patent 5,739,091). Claims 66 - 69, 72 - 74, 76 and 78 - 86 continue to be rejected under 35 U.S.C. §103(a) as unpatentable over Scott (EP 272 923), and claims 66 - 69, 72 - 76 and 78 - 88 remain rejected under 35 U.S.C. §103(a) as obvious over Markussen (EP 304 332). Applicants respectfully traverse each of the above-enumerated rejections.

The Examiner is thanked for the recent brief telephone interview discussing the Examiner's 6/12/01, Office Action paragraph 3 statement that "

"...the invention as claimed does not recite multiple layers. As for the protein matrix surrounding a seed, the granules are prepared by layering the enzyme around dry pre-mix. In regard to the later, applicant cites description of preparation of the referenced granules (col. 4, lines 21-27) which demonstrates that the mix of granule material during preparation is mixed to a homogenous composition. This description, however, does not exclude that the pre-mix serves as a seed and, further, remains in the homogenated composition as a solid (note, that the reference teaches that some of the granule's constituents are insoluble - see col. 1, line 34, line 2, line 66).";

And further discussing the following language in paragraph 3 of the instant 10/15/01

Office Action:

"Claims 66,83 are amended to replace language "protein matrix surrounding the seed particle" with "protein matrix layered over the seed particle". It is obvious, however, that these two phrases are virtually equivalent, as it is apparent that protein matrix can be positioned only around (or over) the seed, as opposed to placing it "into" the seed."

GC507-2AFAM

USSN 09/215,095

Page 5

As is clear from the above quoted language, both Applicants and the Examiner agree that Applicant claims are to a layered granule and the Kiesser et al. granule contains at least some insoluble ingredients that are in a homogenous extrusion composition. The Examiner has stated that claims 66 and 83 were not to multi-layered granules as stated by Applicants. Although a cross section of Applicants' granule would clearly show two distinct regions, nevertheless, independent claims 66 and 83 have been amended to recite an outer barrier or coating.

However, Applicants do not agree that the pre-mix of the Kiesser et al. homogenous composition can constitute a single seed particle that is layered as presently claimed in amended claims 66 and 83. Applicants have attached the Declaration of Nathaniel T. Becker discussing the Kiesser et al. patent.

The Declaration shows that Kiesser et al. teach an extrusion process to prepare an enzyme granule that is not a single seed particle layered over with a protein matrix. An extrusion granule as taught by Kiesser, as opposed to a granule that is prepared by layering a protein matrix over a seed particle, by definition produces a homogeneous mixture with multiple insoluble pre-mix dispersed throughout the granule, on the surface of the granule, and without discrete layers surrounding such multiple insoluble particles. The Kiesser et al. granule does not produce a layered granule having a single seed particle, a layer of protein or enzyme and sugar or sugar alcohol and structuring agent, and an outer barrier or coating.

Applicants' amended claims 66 and 83 are drawn to a single seed particle, a matrix layer surrounding that seed particle and having a structuring agent, and an outer barrier or coating. Support for the amendments to claims 66 and 83 is found 18-20 describing uniform application of the matrix to "individual seed particles"; on page 9, lines 20-28 describing barrier layers and coatings.

Applicants contend the claimed invention is not anticipated by Kiesser et al. To anticipate a claim, the reference must contain all of the elements of the claim. See *Hybritech Inc. v Monoclonal Antibodies, Inc.* 231 USPQ 81 (Fed. Cir. 1986). Missing elements may not be supplied by the knowledge of one skilled in the art or the disclosure of another reference. Additionally, the reference must disclose all of the claimed elements arranged as in the claim and must sufficiently describe the claimed invention to have placed the public in possession of the invention. The reference must contain an

GC507-2AFAM

USSN 09/215,095

Page 6

enabling disclosure. *Scripps Clinic & Research Found. v Genentech, Inc.* 18 USPQ2d 1001 (Fed. Cir. 1991).

The construction and composition of Applicants' enzyme granule is fundamentally different than the enzyme granule taught by Kiesser et al. Applicants' granule is a multi-layered granule including a protein matrix layer, with a structuring agent, layered over a single seed particle. Kiesser et al. do not teach or disclose a granule having a single seed particle surrounded by a matrix layer with a structuring agent. There is nothing in the reference that clearly and unequivocally directs those skilled in the art to make the combination of components of Applicants' granule.

As taught by Kiesser et al. at Column 1, lines 33-39 and column 4, lines 21 - 34, the enzyme granules comprise a homogeneous extrusion composition of an enzyme or enzyme mixture, a water-insoluble filler mixture, water-soluble filler mixtures, binders, if appropriate, other granulating auxiliaries, a formate of an alkali metal or alkaline earth metal and if appropriate reducing sugars. The nexus of the invention is the inclusion in the homogeneous composition of a formate of an alkali metal or alkaline earth metal and the addition of a reducing sugar for stabilization of the formate. Particularly preferred are calcium formate and sodium formate.

Water-insoluble fillers include cellulose, starch, cereal flour and the like (polysaccharides). Water-soluble filler mixtures include inorganic water-soluble salts. There is no disclosure of a sugar as a water-soluble filler.

All of the listed binders are polymers and include polyethylene glycol and polyvinylpyrrolidone. The granule may comprise up to 30% binder. There are no sugars listed as binders. The reference teaches "if" reducing sugars are to be used they include monosaccharides (glucose) disaccharides (lactose/maltose), and polysaccharides (dextrins). These reducing sugars are for synergistic intensification of the stabilizing action of the formate. At column 3, lines 42 - 45, it is taught that the enzyme granule can comprise 0.5 to 15% by weight of a formate and if appropriate 0.5 to 20% by weight of reducing sugar. There is no teaching that sugar and particularly sucrose which is not a reducing sugar could be used in a matrix as claimed by Applicants.

As stated at col. 5, lines 12 - 15 of the reference,

"The enzymes in the granules according to the invention are stabilized in a surprising manner by incorporation of a formate of an alkali metal or alkaline earth metal, if appropriate in combination with a reducing sugar."

GC507-2AFAM

USSN 09/215,095

Page 7

There is no clear and unequivocal teaching in the reference that a protein matrix is comprised of a protein or enzyme mixed together with a combination of a sugar and polysaccharide structuring agent. It is the particular combination of the components of the matrix which circumvent the problem of agglomeration.

Applicants also assert that the invention is not made obvious by the teaching of Kiesser et al. There is no suggestion or motivation provided by Kiesser et al. to make multi-layered enzyme granules having single seed particles and structuring agents. Additionally, the Kiesser et al. reference must include a suggestion or provide a motivation to modify the components of the enzyme mixture in a manner claimed by the Applicants.

The Examiner maintained his 35 U.S.C. §103(a) rejection of claims 75, 76, 80, 81, 87 and 88 as obvious over Scott (EP 272923). As acknowledged by the Examiner, Scott does not teach or suggest a multi-layered granule. The Scott reference is concerned with the problem of the addition of oxygen scavenging food ingredients to prevent oxygen deterioration in food products by either providing a dry free flowing particulate preparation as an effective oxygen scavenger containing glucose (sugar) and glucose oxidase (enzyme), or by providing a dry free flowing particulate preparation which is an effective oxygen scavenger containing glucose oxidase (enzyme), a low molecular weight polysaccharide (maltodextrin) and a hydrolytic enzyme capable of catalyzing the hydrolysis of the polysaccharide into glucose units.

In the first system the glucose and glucose oxidase are combined to form an admixture, but this system does not teach a mixture of a polysaccharide structuring agent mixed with the sugar and enzyme. In the second system the enzyme glucose oxidase is combined with a low weight polysaccharide and a second enzyme wherein the second enzyme can catalyze the hydrolysis of the polysaccharide into glucose units. This system while including an enzyme and a polysaccharide is devoid of teaching a sugar mixed with the enzyme and polysaccharide. Applicants' multi-layered enzyme granulate is not made obvious by the particulate enzyme composition as disclosed by Scott. The reference particles do not suggest either explicitly or implicitly the instantly claimed granules wherein an enzyme is admixed with a combination of a sugar or sugar alcohol and a polysaccharide structuring agent.

GC507-2AFAM

USSN 09/215,095

Page 8


The Examiner has also rejected Applicants' claims 66-69, 72-76, 78-88 as obvious over Markussen (EP 304332). Applicants granule is different from and not obvious over Markussen. Applicants core is a single seed particle, and the layer surrounding the seed particle is a matrix of the protein or enzyme, sugar and structuring agent. Markussen teaches a core having a protein in the core and a coating either with or without a protein. In another embodiment, the core does not have a protein but a coating which includes cellulose fibers or artificial fibers, a binder, a filler, one or more granulating agents and an enzyme. The binders are disclosed as polymer compounds. There is no teaching of forming a matrix of the protein or enzyme, sugar and polysaccharide compound. The fact that the core could include a sugar, starch or protein is not a disclosure sufficient to teach or suggest a layer around a single seed particle wherein the layer is a matrix comprising a mixture of a protein, sugar and soluble structuring agent.

Applicants contend instant claims 66 - 88 and added claims 89-98 are patentable over the cited references, and withdrawal of all pending rejections is respectfully requested. Allowance of the claims is kindly solicited. If in the opinion of the Examiner a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 846-4072.

Respectfully submitted,

Date:

12/17/01



Janet Kaiser Castaneda
Registration No. 33,228
Attorney for Applicants

Genencor International, Inc.
925 Page Mill Road
Palo Alto, CA 94304-1013
Tel: 650-846-4072
Fax: 650-845-6504

Enclosure: Marked-up version of amended claims

GC507-2AFAM

USSN 09/215,095

Page 9

VERSION SHOWING CHANGES MADE

66.(Twice amended) A granule comprising,

- c) an individual seed particle; [and]
- d) a protein matrix layered over the seed particle wherein said matrix includes a protein mixed together with a combination of a sugar or sugar alcohol and a polysaccharide structuring agent; and
- c) an outer barrier or coating.

78. (amended) The granule of claim 66 [further comprising a] having a coating layered over the protein matrix.

83. (Twice amended) An enzyme granule comprising,

- a) an individual seed particle; [and]
- b) an enzyme matrix layered over the seed particle wherein said matrix includes an enzyme mixed together with a combination of a sugar and a polysaccharide structuring agent, said enzyme selected from the group consisting of proteases, amylases, lipases and cellulases and said polysaccharide structuring agent selected from the group consisting of starch, modified starch, cellulose, modified cellulose, carrageenan, gum Arabic, xanthan gum, locust bean gum, and guar gum; and
- c) an outer barrier or coating.

84. (amended) The enzyme granule of claim 85 [further comprising a] having a coating layered over the enzyme matrix.

I hereby certify that this correspondence is being sent by facsimile transmission in accordance with § 1.6(d) addressed to Art Unit 1631, Facsimile No. 703-872-9307, Commissioner for Patents, Washington, D.C. 20231 on the date shown below.

Date: December 17, 2001

By: Carol A. See

Carol A. See

PATENT

Docket No. GC507-2

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of

N. T. Becker et al.

Serial No.: 09/215,095

Filed: December 18, 1998

For: MATRIX GRANULE

)
)
) Group Art Unit: 1631

)
) Examiner: Michael Borin

DECLARATION OF NATHANIEL T. BECKER UNDER 37 CFR §1.132

1. I, Nathaniel T. Becker, declare as follows under penalty of perjury.
2. I hold a Bachelor of Science Degree in Chemical Engineering from Stanford University, awarded in 1983, and a Master of Science Degree from University of California, Davis, awarded in 1984.
3. Since 1983, I have worked continually in the fields of biochemical engineering, including, enzyme research, such as research in enzyme formulations, stabilization, granulation, coatings, and enzyme release technologies. I have been employed at Genencor International, Inc. since 1985. Currently, I am the Group Leader for the Delivery Systems group where I develop liquid and solid enzyme formulations. I have attached a C.V. to this Declaration.
4. In the course of my employment outlined above, I have been continuously involved with the design and formulation of enzyme granules using a variety of enzymes and other materials, such as starches, binders, core materials, coatings, and sugars.
5. I have read U.S. Patent Nos. 5,739,091 (Kiesser et al.); EP 272923 (Scott); and EP 304332 (Martussen). I am familiar with the granules described in the Kiesser et al., Scott, and Martussen et al. patents.
6. I have reviewed the U.S. Pat. Office Actions dated June 12, 2001, and October 15, 2001. The June 12, 2001, Office Action contains the following statement:

GC507-2AFAM

09/215,095

"...the invention as claimed does not recite multiple layers. As for the protein matrix surrounding a seed, the granules are prepared by layering the enzyme around dry pre-mix. In regard to the later, applicant cites description of preparation of the referenced granules (col. 4, lines 21-27) which demonstrates that the mix of granule material during preparation is mixed to a homogenous composition. This description, however, does not exclude that the pre-mix serves as a seed and, further, remains in the homogenated composition as a solid (note, that the reference teaches that some of the granule's constituents are insoluble - see col. 1, line 34, line 2, line 66)."

7. The above statements that the homogenous composition of Kiesser et al. does not exclude that the pre-mix serves as a seed is incorrect as applied to Applicants' layered seed particles. By definition, and as is recognized by those skilled in the art, an extrusion product is a homogenous mixture with any particulate matter dispersed throughout the entire mixture, including on or at the surface of the mixture. The Kiesser extruded granule necessarily has multiple insoluble particles from the pre-mix scattered throughout the entire interior region of the granule and at the surface of the granule. The Kiesser insoluble pre-mix, particularly the pre-mix at the surface of the granule, is not surrounded by a layer. The Examiner is referred to Column 4, lines 21-34.
8. Kiesser et al. also does not use sugars as binders. Kiesser teaches "if" reducing sugars are to be used they include monosaccharides (glucose) disaccharides (lactose/maltose), and polysaccharides (dextrins). These reducing sugars are for synergistic intensification of the stabilizing action of the formate. At column 3, lines 42 - 45, it is taught that the enzyme granule can comprise 0.5 to 15% by weight of a formate and if appropriate 0.5 to 20% by weight of reducing sugar. Kiesser teaches only reducing sugars and sucrose, listed as an example of Applicant's non-reducing sugars, is not a reducing sugar.
9. Those skilled in the art would not find Applicants' invention obvious over Kiesser et al. since Kiesser's granule is an extrusion product without a single seed particle core coated with a first layer of a protein or enzyme matrix and a second outer barrier or coating.
10. The Scott (EP 272923) patent does not teach a multi-layered granule and the Examiner acknowledged this fact. Scott addressed the

09/215,095

problem of preventing oxygen deterioration in food products by providing a dry free flowing particulate preparation as an effective oxygen scavenger. Scott has either an enzyme sugar mixture or an enzyme polysaccharide mixture. Scott does not teach or suggest a matrix of a polysaccharide structuring agent mixed with sugar and enzyme. Applicants' multi-layered enzyme granulate is not made obvious by the particulate enzyme composition as disclosed by Scott.

11. Markussen teaches a protein core and a coating either with or without protein. In another embodiment, the core does not have a protein but the coating requires cellulose fibers or artificial fibers, a binder, a filler, one or more granulating agents and an enzyme. The binders are disclosed as polymer compounds. There is no teaching of forming a matrix of the protein or enzyme, sugar and polysaccharide compound. The fact that the core could include a sugar, starch or protein is not sufficient to teach or suggest to those skilled in the art a multi-layered granule having a layer around a single seed particle where the layer is a matrix comprising a mixture of a protein, sugar and structuring agent.

12. None of the references, alone or in combination, would suggest to those skilled in the art Applicants' invention.

Respectfully submitted,

Nathaniel T. Becker

12/17/01

Nathaniel T. Becker